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NEWS 1		Web Page for STN Seminar Schedule - N. America
NEWS 2	MAR 15	WPIDS/WPIX enhanced with new FRAGHITSTR display format
NEWS 3	MAR 16	CASREACT coverage extended
NEWS 4	MAR 20	MARPAT now updated daily
NEWS 5	MAR 22	LWPI reloaded
NEWS 6	MAR 30	RDISCLOSURE reloaded with enhancements
NEWS 7	APR 02	JICST-EPLUS removed from database clusters and STN
NEWS 8	APR 30	GENBANK reloaded and enhanced with Genome Project ID field
NEWS 9	APR 30	CHEMCATS enhanced with 1.2 million new records
NEWS 10	APR 30	CA/CAplus enhanced with 1870-1889 U.S. patent records
NEWS 11	APR 30	INPADOC replaced by INPADOCDB on STN
NEWS 12	MAY 01	New CAS web site launched
NEWS 13	MAY 08	CA/CAplus Indian patent publication number format defined
NEWS 14	MAY 14	RDISCLOSURE on STN Easy enhanced with new search and display fields
NEWS 15	MAY 21	BIOSIS reloaded and enhanced with archival data
NEWS 16	MAY 21	TOXCENTER enhanced with BIOSIS reload
NEWS 17	MAY 21	CA/CAplus enhanced with additional kind codes for German patents
NEWS 18	MAY 22	CA/CAplus enhanced with IPC reclassification in Japanese patents
NEWS 19	JUN 27	CA/CAplus enhanced with pre-1967 CAS Registry Numbers
NEWS 20	JUN 29	STN Viewer now available
NEWS 21	JUN 29	STN Express, Version 8.2, now available
NEWS 22	JUL 02	LEMBASE coverage updated
NEWS 23	JUL 02	LMEDLINE coverage updated
NEWS 24	JUL 02	SCISEARCH enhanced with complete author names
NEWS 25	JUL 02	CHEMCATS accession numbers revised
NEWS 26	JUL 02	CA/CAplus enhanced with utility model patents from China

NEWS EXPRESS 29 JUNE 2007: CURRENT WINDOWS VERSION IS V8.2,
CURRENT MACINTOSH VERSION IS V6.0c(ENG) AND V6.0Jc(JP),
AND CURRENT DISCOVER FILE IS DATED 4 MAY 2007.

NEWS HOURS	STN Operating Hours Plus Help Desk Availability
NEWS LOGIN	Welcome Banner and News Items
NEWS IPC8	For general information regarding STN implementation of IPC 8

Enter NEWS followed by the item number or name to see news on that specific topic.

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* * * * * * * * * * * * * * * * STN Columbus * * * * * * * * * * * * * * * *

FILE 'HOME' ENTERED AT 11:16:18 ON 02 JUL 2007

=> file reg

COST IN U.S. DOLLARS	SINCE FILE ENTRY	TOTAL SESSION
FULL ESTIMATED COST	0.21	0.21

FILE 'REGISTRY' ENTERED AT 11:16:27 ON 02 JUL 2007

Property values tagged with IC are from the ZIC/VINITI data file provided by InfoChem.

STRUCTURE FILE UPDATES: 1 JUL 2007 HIGHEST RN 940612-32-8
DICTIONARY FILE UPDATES: 1 JUL 2007 HIGHEST RN 940612-32-8

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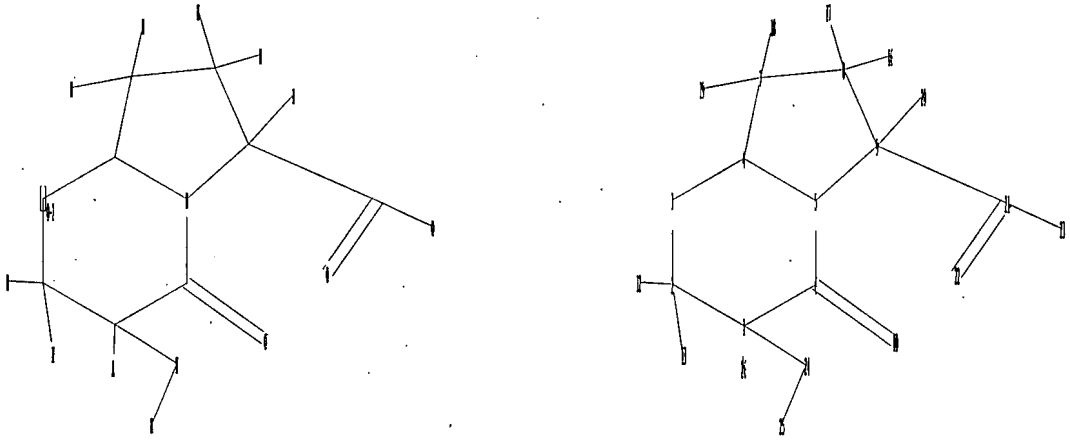
TSCA INFORMATION NOW CURRENT THROUGH December 2, 2006

Please note that search-term pricing does apply when conducting SmartSELECT searches.

REGISTRY includes numerically searchable data for experimental and predicted properties as well as tags indicating availability of experimental property data in the original document. For information on property searching in REGISTRY, refer to:

http://www.cas.org/support/stngen/stndoc/properties.html

=>
Uploading C:\Program Files\Stnexp\Queries\10563288a.str



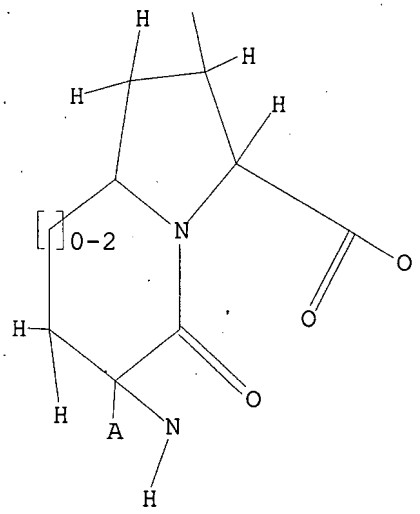
chain nodes :
10 12 13 16 17 18 19 20 21 22 23 24 25 26
ring nodes :
1 2 3 4 5 6 7 8 9
chain bonds :
1-24 1-26 2-12 2-13 6-10 7-18 7-19 8-16 8-17 9-20 9-21 21-22 21-23 24-25
ring bonds :
1-2 1-6 2-3 3-4 4-5 4-7 5-6 5-9 7-8 8-9
exact/norm bonds :
1-2 1-6 1-24 1-26 2-3 3-4 4-5 5-6 5-9 6-10 21-22 21-23
exact bonds :
2-12 2-13 4-7 7-8 7-18 7-19 8-9 8-16 8-17 9-20 9-21 24-25
isolated ring systems :

containing 1 :

Match level :
1:Atom 2:Atom 3:Atom 4:Atom 5:Atom 6:Atom 7:Atom 8:Atom 9:Atom 10:CLASS
12:CLASS 13:CLASS 16:CLASS 17:CLASS 18:CLASS 19:CLASS 20:CLASS 21:CLASS
22:CLASS 23:CLASS 24:CLASS 25:CLASS 26:CLASS

L1 STRUCTURE UPLOADED

=> d l1
L1 HAS NO ANSWERS
L1 STR



Structure attributes must be viewed using STN Express query preparation.

=> s l1 full
FULL SEARCH INITIATED 11:16:46 FILE 'REGISTRY'
FULL SCREEN SEARCH COMPLETED - 2321 TO ITERATE

100.0% PROCESSED 2321 ITERATIONS 43 ANSWERS
SEARCH TIME: 00.00.01

L2 43 SEA SSS FUL L1

=> file caplus
COST IN U.S. DOLLARS

	SINCE FILE ENTRY	TOTAL SESSION
FULL ESTIMATED COST	172.10	172.31

FILE 'CAPLUS' ENTERED AT 11:16:54 ON 02 JUL 2007
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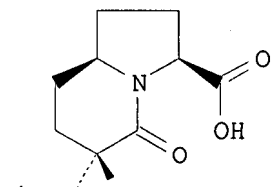
FILE COVERS 1907 - 2 Jul 2007 VOL 147 ISS 2
FILE LAST UPDATED: 1 Jul 2007 (20070701/ED)

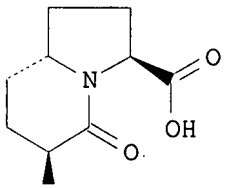

```
=> s l2 full
L3          18 L2

=> s l3 and py<2003
      22885672 PY<2003
L4          13 L3 AND PY<2003

=> d ibib abs hitstr tot
```

L4 ANSWER 1 OF 13 CAPLUS COPYRIGHT 2007 ACS on STN

ACCESSION NUMBER: 2003:69868 CAPLUS
DOCUMENT NUMBER: 139:53275
TITLE: Cyclic RGD peptides containing azabicycloalkane reverse-turn mimics
AUTHOR(S): Belvisi, Laura; Caporale, Andrea; Colombo, Matteo; Manzoni, Leonardo; Potenza, Donatella; Scolastico, Carlo; Castorina, Massimo; Cati, Matilde; Giannini, Giuseppe; Pisano, Claudio
CORPORATE SOURCE: Dipartimento di Chimica Organica e Industriale, Universita degli Studi di Milano, Milan, I-20133, Italy
SOURCE: Helvetica Chimica Acta (2002), 85(12), 4353-4368
CODEN: HCACAV; ISSN: 0018-019X
PUBLISHER: Verlag Helvetica Chimica Acta
DOCUMENT TYPE: Journal
LANGUAGE: English
OTHER SOURCE(S): CASREACT 139:53275
GI



I



II

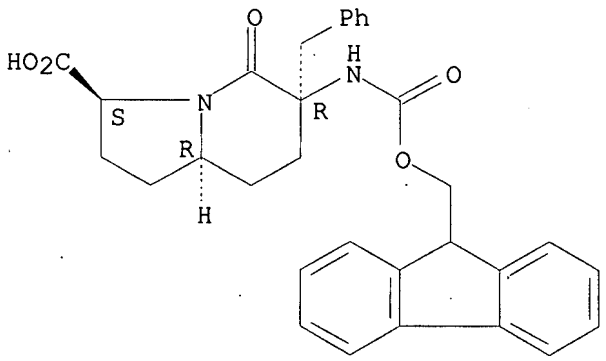
AB The Fmoc-protected lactams I and II were used to prepare cyclo(Arg-Gly-Asp-lactam) (III) and cyclo(Arg-Gly-Asp-Phe-lactam), which contain the Arg-Gly-Asp (RGD) recognition motif. Their solid-phase synthesis, conformational anal., and binding to purified αvβ3 and αvβ5 integrins are reported. Compound III was found to act as an active and selective inhibitor of the αvβ5 integrin.

IT 220719-80-2
RL: RCT (Reactant); RACT (Reactant or reagent)
(solid-phase synthesis, conformational anal., and integrin-binding of cyclic RGD peptides containing azabicycloalkane reverse-turn mimics)

RN 220719-80-2 CAPLUS

CN 3-Indolizinecarboxylic acid, 6-[[(9H-fluoren-9-ylmethoxy)carbonyl]amino]octahydro-5-oxo-6-(phenylmethyl)-, (3S,6R,8aR)-(9CI) (CA INDEX NAME)

Absolute stereochemistry.



REFERENCE COUNT: 49 THERE ARE 49 CITED REFERENCES AVAILABLE FOR THIS RECORD. ALL CITATIONS AVAILABLE IN THE RE FORMAT

L4 ANSWER 2 OF 13 CAPLUS COPYRIGHT 2007 ACS on STN
ACCESSION NUMBER: 1999:529170 CAPLUS
DOCUMENT NUMBER: 131:157992
TITLE: Synthesis of β-sheet mimetics as inhibitors of protease, kinase, transcription factors, and protein-protein binding interactions
INVENTOR(S): Qaber, Maher N.; McMillian, Michael K.; Kahn, Michael S.; Tulinsky, John E.; Mathew, Jessymol
PATENT ASSIGNEE(S): Molecumetics Ltd., USA
SOURCE: PCT Int. Appl., 279 pp.
CODEN: PIXXD2
DOCUMENT TYPE: Patent
LANGUAGE: English
FAMILY ACC. NUM. COUNT: 1
PATENT INFORMATION:

PATENT NO.	KIND	DATE	APPLICATION NO.	DATE
WO 9941276	A1	19990819	WO 1998-US2891	19980212 <--
W: AL, AM, AT, AU, BA, BB, BG, BR, BY, CA, CH, CN, CU, CZ, DE, DK, EE, ES, FI, GB, GE, GH, GM, GW, HU, ID, IL, IS, JP, KE, KG, KP, KR, KZ, LC, LK, LR, LS, LT, LU, LV, MD, MG, MK, MN, MW, MX, NO, NZ, PL, PT, RO, RU, SD, SE, SG, SI, SK, SL, TJ, TM, TR, TT, UA, UG, US, UZ, VN, YU, ZW, AM, AZ, BY, KG, KZ, MD, RU, TJ, TM				
RW: GH, GM, KE, LS, MW, SD, SZ, UG, ZW, AT, BE, CH, DE, DK, ES, FI, FR, GB, GR, IE, IT, LU, MC, NL, PT, SE, BF, BJ, CF, CG, CI, CM, GA, GN, ML, MR, NE, SN, TD, TG				
CA 2319766	A1	19990819	CA 1998-2319766	19980212 <--
AU 9866557	A	19990830	AU 1998-66557	19980212 <--
AU 748887	B2	20020613		
EP 1053246	A1	20001122	EP 1998-908551	19980212 <--
EP 1053246	B1	20030102		
R: AT, BE, CH, DE, DK, ES, FR, GB, GR, IT, LI, LU, NL, SE, MC, PT, IE, FI				
JP 2002503674	T	20020205	JP 2000-531467	19980212 <--
AT 230414	T	20030115	AT 1998-908551	19980212
NZ 505980	A	20030131	NZ 1998-505980	19980212
ES 2192764	T3	20031016	ES 1998-908551	19980212
PRIORITY APPLN. INFO.:			WO 1998-US2891 A	19980212

OTHER SOURCE(S): MARPAT 131:157992
GI

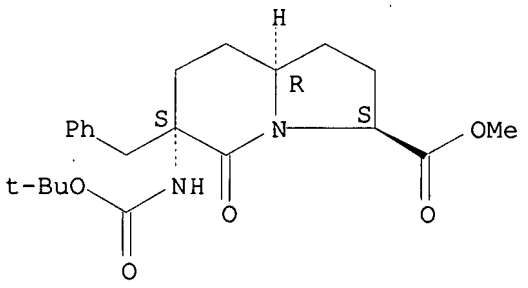
* STRUCTURE DIAGRAM TOO LARGE FOR DISPLAY - AVAILABLE VIA OFFLINE PRINT *

AB β-Sheet mimetics I [A = CO, (CH2)0-4, CO(CH2)1-3, (CH2)1-2O, (CH2)1-2S; B = N, CH; C = CO, CO(CH2)1-3, (CH2)0-3, O, S, O(CH2)1-2, S(CH2)1-2; D = N, CR4; E = CR1(NHZ), NZ, CZR1; F is an optional carbonyl moiety; R1, R3, R4 is an amino acid side chain moiety or derivative; R2, R2' are ring substituents selected from an amino acid side chain moiety or derivative, where at least one R2 together with C forms a fused (un)substituted homo- or heterocyclic ring; Y, Z represent the remainder of the mol.; any adjacent CH groups of the bicyclic ring may form a double bond] were prepared as inhibitors of protease, kinase, transcription factors, and protein-protein binding interactions. Thus, arginine derivative II was prepared and assayed for inhibition of various enzymes (IC50 = 1.2 and 140 nM for thrombin and Factor VII, resp.).

IT 183442-92-4P 183442-93-5P 183624-03-5P
RL: RCT (Reactant); SPN (Synthetic preparation); PREP (Preparation); RACT (Reactant or reagent)
(synthesis of β-sheet mimetics as inhibitors of protease, kinase, transcription factors, and protein-protein binding interactions)

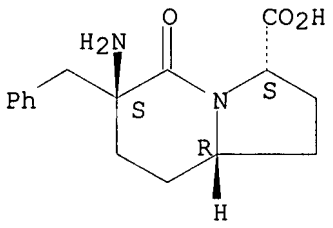
RN 183442-92-4 CAPLUS
CN 3-Indolizinecarboxylic acid, 6-[[(1,1-dimethylethoxy)carbonyl]amino]octahydro-5-oxo-6-(phenylmethyl)-, methyl ester, (3R,6R,8aS)-rel- (9CI) (CA INDEX NAME)

Relative stereochemistry.



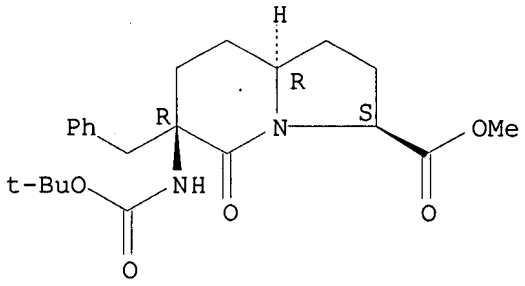
RN 183442-93-5 CAPLUS
CN 3-Indolizinecarboxylic acid, 6-aminooctahydro-5-oxo-6-(phenylmethyl)-, (3R,6R,8aS)-rel- (9CI) (CA INDEX NAME)

Relative stereochemistry.



RN 183624-03-5 CAPLUS
CN 3-Indolizinecarboxylic acid, 6-[[(1,1-dimethylethoxy)carbonyl]amino]octahydro-5-oxo-6-(phenylmethyl)-, methyl ester, (3R,6S,8aS)-rel- (9CI) (CA INDEX NAME)

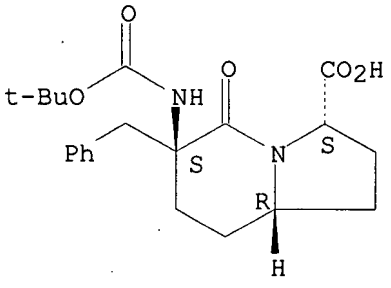
Relative stereochemistry.



REFERENCE COUNT: 7 THERE ARE 7 CITED REFERENCES AVAILABLE FOR THIS RECORD. ALL CITATIONS AVAILABLE IN THE RE FORMAT

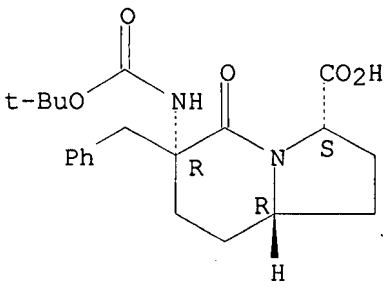
L4 ANSWER 3 OF 13 CAPLUS COPYRIGHT 2007 ACS on STN
ACCESSION NUMBER: 1999:396495 CAPLUS
DOCUMENT NUMBER: 131:200003
TITLE: Synthesis of dipeptide secondary structure mimetics
AUTHOR(S): Eguchi, Masakatsu; Kim, Hwa-Ok; Gardner, Benjamin S.; Boatman, P. Douglas; Lee, Min S.; Nakanishi, Hiroshi; Kahn, Michael
CORPORATE SOURCE: Molecumetics Ltd., Bellevue, WA, 98005, USA
SOURCE: Peptides: Frontiers of Peptide Science, Proceedings of the American Peptide Symposium, 15th, Nashville, June 14-19, 1997 (1999), Meeting Date 1997, 212-213. Editor(s): Tam, James P.; Kaumaya, Pravin T. P. Kluwer: Dordrecht, Neth.
CODEN: 67UCAR
DOCUMENT TYPE: Conference
LANGUAGE: English
AB A symposium with four refs. on the synthesis and biol. activity of two diastereomeric title compds.
IT 203453-44-5P 203455-60-1P
RL: RCT (Reactant); SPN (Synthetic preparation); PREP (Preparation); RACT (Reactant or reagent)
(preparation and reaction of in the synthesis of dipeptide secondary structure mimetics as thrombin inhibitors)
RN 203453-44-5 CAPLUS
CN 3-Indolizinecarboxylic acid, 6-[[(1,1-dimethylethoxy)carbonyl]amino]octahydro-5-oxo-6-(phenylmethyl)-, (3S,6S,8aR)- (9CI) (CA INDEX NAME)

Absolute stereochemistry.



RN 203455-60-1 CAPLUS
CN 3-Indolizinecarboxylic acid, 6-[[(1,1-dimethylethoxy)carbonyl]amino]octahydro-5-oxo-6-(phenylmethyl)-, (3S,6R,8aR)- (9CI) (CA INDEX NAME)

Absolute stereochemistry.



REFERENCE COUNT: 4 THERE ARE 4 CITED REFERENCES AVAILABLE FOR THIS RECORD. ALL CITATIONS AVAILABLE IN THE RE FORMAT

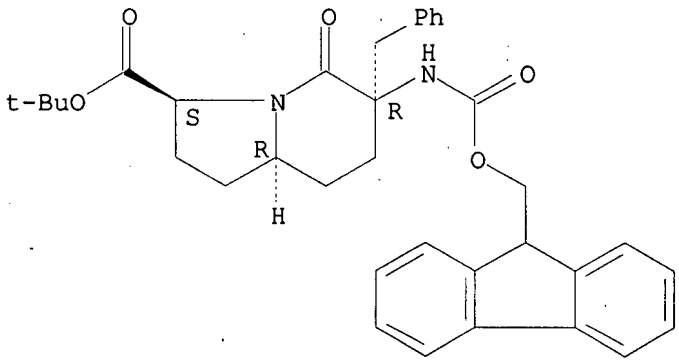
L4 ANSWER 4 OF 13 CAPLUS COPYRIGHT 2007 ACS on STN
ACCESSION NUMBER: 1999:89647 CAPLUS
DOCUMENT NUMBER: 130:182766
TITLE: Conformational preferences of peptides containing reverse-turn mimetic bicyclic lactams. Inverse γ-turns versus type-II' β-turns. Insights into β-hairpin stability
AUTHOR(S): Belvisi, Laura; Gennari, Cesare; Mielgo, Antonia; Potenza, Donatella; Scolastico, Carlo
CORPORATE SOURCE: Dipartimento Chimica Organica Industriale, Univ. Studi Milano, Milan, Italy
SOURCE: European Journal of Organic Chemistry (1999), (2), 389-400
CODEN: EJOCFK; ISSN: 1434-193X
PUBLISHER: Wiley-VCH Verlag GmbH
DOCUMENT TYPE: Journal
LANGUAGE: English

AB The conformational preferences of constrained peptides containing reverse-turn mimetic bicyclic lactams were investigated by NMR and IR. The exptl. results were complemented by computer modeling studies and show that the constrained peptides form an inverse γ-turn or a type-II' β-turn through intramol. H-bonding, depending on the nature of the reverse-turn mimic. In N-acetylated tetrapeptide mimics incorporating the two different bicyclic lactams, H(5) is available for either a γ-turn (7-membered ring with the CO group of the bicyclic lactam) or a β-turn (10-membered ring with the CO group of residue 2). Peptides incorporating a (5,7)-bicyclic lactam predominantly induce the γ-turn conformation, while those incorporating a (5,6)-bicyclic lactam can promote either a γ-turn or a β-turn conformation, with the β-turn usually being preferred and with varying degrees of β-hairpin formation.

IT 220563-70-2
RL: PRP (Properties)
(conformational anal.)

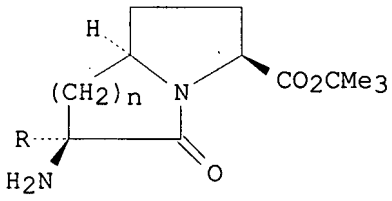
RN 220563-70-2 CAPLUS
CN 3-Indolizinecarboxylic acid, 6-[[(9H-fluoren-9-ylmethoxy)carbonyl]amino]octahydro-5-oxo-6-(phenylmethyl)-, 1,1-dimethylethyl ester, (3S,6R,8aR)- (9CI) (CA INDEX NAME)

Absolute stereochemistry. Rotation (+).



REFERENCE COUNT: 68 THERE ARE 68 CITED REFERENCES AVAILABLE FOR THIS RECORD. ALL CITATIONS AVAILABLE IN THE RE FORMAT

L4 ANSWER 5 OF 13 CAPLUS COPYRIGHT 2007 ACS on STN
ACCESSION NUMBER: 1999:89646 CAPLUS
DOCUMENT NUMBER: 130:196946
TITLE: Solid-phase synthesis of peptides containing reverse-turn mimetic bicyclic lactams
AUTHOR(S): Gennari, Cesare; Mielgo, Antonia; Potenza, Donatella; Scolastico, Carlo; Piarulli, Umberto; Manzoni, Leonardo
CORPORATE SOURCE: Dipartimento Chimica Organica Industriale, Univ. Studi Milano, Milan, Italy
SOURCE: European Journal of Organic Chemistry (1999), (2), 379-388
CODEN: EJOCFK; ISSN: 1434-193X
PUBLISHER: Wiley-VCH Verlag GmbH
DOCUMENT TYPE: Journal
LANGUAGE: English
GI



I

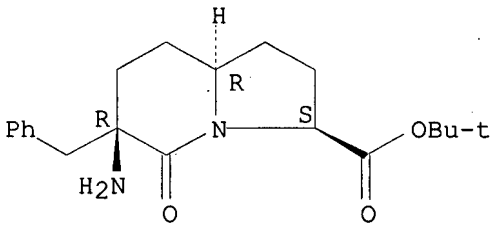
AB The solid-phase synthesis and characterization of a series of peptides containing reverse-turn mimetic bicyclic lactams I (n = 3, R = H; n = 2, R = PhCH2) is reported. The bicyclic lactams possess high structural similarity to the 2 central residues of a β-turn. Amino acid conjugates of these bicyclic lactams were synthesized on solid supports following a 9-fluorenylmethoxycarbonyl (FMOC) protection strategy on Wang-Merrifield resin. Coupling between amino acids was accomplished by diisopropylcarbodiimide (DIC)/hydroxyazabenzotriazole (HOAt). Coupling between amino acids and the mimics was performed with the potent Carpino's reagent, O-(7-azabenzotriazol-1-yl)-N,N,N',N'-tetramethyluronium hexafluorophosphate (HATU). The final compds. were cleaved from the resin and obtained as N-acetylated Me esters or benzyl amides.

IT 208455-27-0
RL: RCT (Reactant); RACT (Reactant or reagent)
(solid-phase synthesis of peptides containing reverse-turn mimetic bicyclic lactams)

RN 208455-27-0 CAPLUS

CN 3-Indolizinecarboxylic acid, 6-aminooctahydro-5-oxo-6-(phenylmethyl)-, 1,1-dimethylethyl ester, (3S,6R,8aR)- (9CI) (CA INDEX NAME)

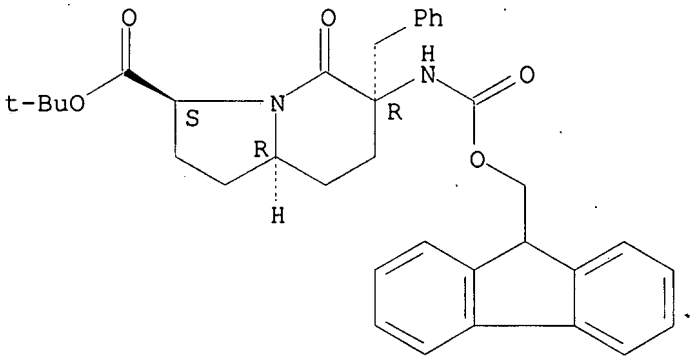
Absolute stereochemistry. Rotation (-).



IT 220563-70-2P 220719-80-2P
RL: RCT (Reactant); SPN (Synthetic preparation); PREP (Preparation); RACT (Reactant or reagent)
(solid-phase synthesis of peptides containing reverse-turn mimetic bicyclic lactams)

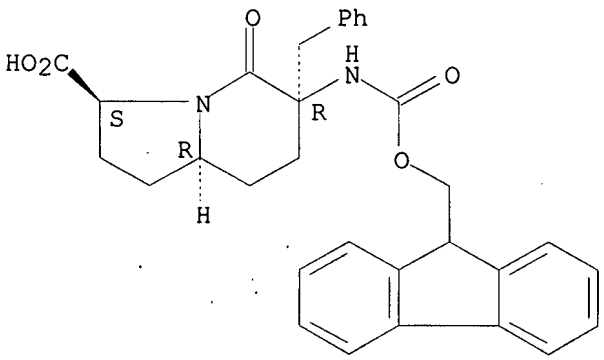
RN 220563-70-2 CAPLUS
CN 3-Indolizinecarboxylic acid, 6-[[(9H-fluoren-9-ylmethoxy)carbonyl]amino]octahydro-5-oxo-6-(phenylmethyl)-, 1,1-dimethylethyl ester, (3S,6R,8aR)- (9CI) (CA INDEX NAME)

Absolute stereochemistry. Rotation (+).



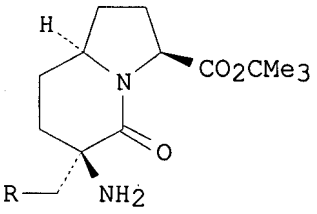
RN 220719-80-2 CAPLUS
CN 3-Indolizinecarboxylic acid, 6-[[(9H-fluoren-9-ylmethoxy)carbonyl]amino]octahydro-5-oxo-6-(phenylmethyl)-, (3S,6R,8aR)- (9CI) (CA INDEX NAME)

Absolute stereochemistry.



REFERENCE COUNT: 90 THERE ARE 90 CITED REFERENCES AVAILABLE FOR THIS

L4 ANSWER 6 OF 13 CAPLUS COPYRIGHT 2007 ACS on STN
ACCESSION NUMBER: 1998:304016 CAPLUS
DOCUMENT NUMBER: 129:41402
TITLE: Stereoselective synthesis of 6,5-bicyclic reverse-turn peptidomimetics
AUTHOR(S): Colombo, Lino; Di Giacomo, Marcello; Brusotti, Gloria; Sardone, Nicola; Angiolini, Mauro; Belvisi, Laura; Maffioli, Sonia; Manzoni, Leonardo; Scolastico, Carlo
CORPORATE SOURCE: Pharmaceutical Chemistry Department, University of Pavia, Pavia, 27100, Italy
SOURCE: Tetrahedron (1998), 54(20), 5325-5336
CODEN: TETRAB; ISSN: 0040-4020
PUBLISHER: Elsevier Science Ltd.
DOCUMENT TYPE: Journal
LANGUAGE: English
OTHER SOURCE(S): CASREACT 129:41402
GI



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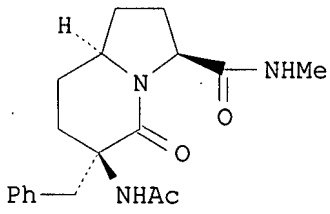


II

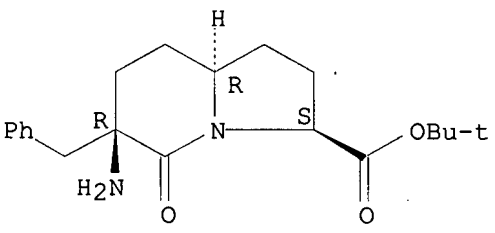
AB A flexible stereoselective synthetic scheme was developed to prepare 6,5-fused bicyclic lactams I (R = Ph, 1-naphthyl, 2-naphthyl), that mol. mechanics calcns. revealed to have a potential as reverse-turn mimetics. The convergence of the synthetic sequence was achieved by attachment of a properly substituted malonate unit RCH2CH(CO2H)CO2Me to (2S)-cis-5-(2-hydroxyethyl)proline tert-Bu ester. Stereoselective intramol. alkylation of the malonate afforded the 6-membered lactam fused to the 2-carbalkoxy pyrrolidine nucleus. X-ray crystallog. of advanced synthetic derivative II allowed the unequivocal assignment of the configuration at the newly created quaternary stereocenter as R.

IT 208455-27-0P
RL: RCT (Reactant); SPN (Synthetic preparation); PREP (Preparation); RACT (Reactant or reagent)
(stereoselective synthesis of bicyclic reverse-turn peptidomimetics)

RN 208455-27-0 CAPLUS

CN 3-Indolizinecarboxylic acid, 6-aminooctahydro-5-oxo-6-(phenylmethyl)-, 1,1-dimethylethyl ester, (3S,6R,8aR)- (9CI) (CA INDEX NAME)

Absolute stereochemistry. Rotation (-).

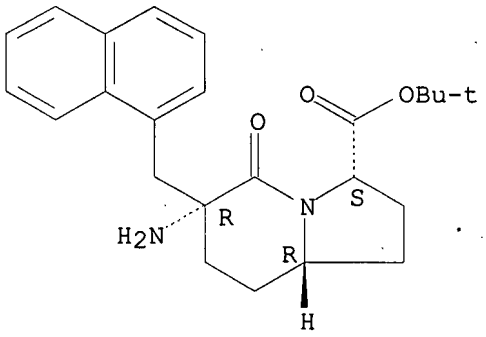


IT 208455-28-1P 208455-29-2P
RL: SPN (Synthetic preparation); PREP (Preparation)
(stereoselective synthesis of bicyclic reverse-turn peptidomimetics)

RN 208455-28-1 CAPLUS

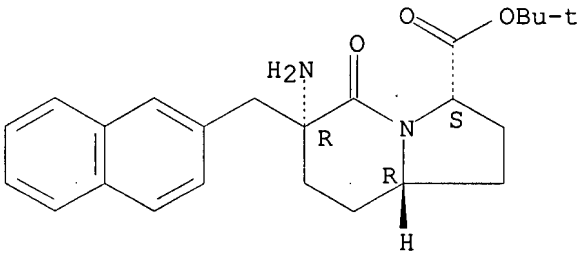
CN 3-Indolizinecarboxylic acid, 6-aminooctahydro-6-(1-naphthalenylmethyl)-5-oxo-, 1,1-dimethylethyl ester, (3S,6R,8aR)- (9CI) (CA INDEX NAME)

Absolute stereochemistry. Rotation (-).



RN 208455-29-2 CAPLUS
CN 3-Indolizinecarboxylic acid, 6-aminooctahydro-6-(2-naphthalenylmethyl)-5-oxo-, 1,1-dimethylethyl ester, (3S,6R,8aR)- (9CI) (CA INDEX NAME)

Absolute stereochemistry. Rotation (-).



REFERENCE COUNT: 9 THERE ARE 9 CITED REFERENCES AVAILABLE FOR THIS RECORD. ALL CITATIONS AVAILABLE IN THE RE FORMAT

L4 ANSWER 7 OF 13 CAPLUS COPYRIGHT 2007 ACS on STN
ACCESSION NUMBER: 1998:112235 CAPLUS
DOCUMENT NUMBER: 128:192934
TITLE: Preparation of peptide β-sheet mimetics as protease and kinase inhibitors and as inhibitors of transcription factors
INVENTOR(S): Kahn, Michael; Qabar, Maher Nicola; McMillan, Michael Kim; Ogbu, Cyprian Okwara; Eguchi, Masakatsu; Kim, Hwa-ok; Boatman, Patrick Douglas, Jr.; Urban, Jan; et al.
PATENT ASSIGNEE(S): Molecumetics Ltd., USA
SOURCE: PCT Int. Appl., 250 pp.
CODEN: PIXXD2
DOCUMENT TYPE: Patent
LANGUAGE: English
FAMILY ACC. NUM. COUNT: 3
PATENT INFORMATION:

PATENT NO.	KIND	DATE	APPLICATION NO.	DATE
WO 9805333	A1	19980212	WO 1997-US13622	19970805 <--

W: AL, AM, AT, AU, BA, BB, BG, BR, BY, CA, CH, CN, CU, CZ, DE, DK, EE, ES, FI, GB, GE, GH, HU, IL, IS, JP, KE, KG, KP, KR, KZ, LC, LK, LR, LS, LT, LU, LV, MD, MG, MK, MN, MW, MX, NO, NZ, PL, PT, RO, RU, SD, SE, SG, SI, SK, TJ, TM, TR, TT, UA, UG, US, UZ, VN, YU, AZ

RW: GH, KE, LS, MW, SD, SZ, UG, ZW, AT, BE, CH, DE, DK, ES, FI, FR, GB, GR, IE, IT, LU, MC, NL, PT, SE, BF, BJ, CF, CG, CI, CM, GA, GN, ML, MR, NE, SN, TD, TG					
CA 2262900	A1	19980212	CA 1997-2262900		19970805 <--
AU 9739058	A	19980225	AU 1997-39058		19970805 <--
AU 732174	B2	20010412			
EP 915700	A1	19990519	EP 1997-936371		19970805 <--
EP 915700	B1	20060322			
R: AT, BE, CH, DE, DK, ES, FR, GB, GR, IT, LI, LU, NL, SE, MC, PT, IE, FI					
NZ 334227	A	20001027	NZ 1997-334227		19970805 <--
JP 2001524931	T	20011204	JP 1998-508118		19970805 <--
AT 320811	T	20060415	AT 1997-936371		19970805
EP 1661566	A2	20060531	EP 2006-130		19970805
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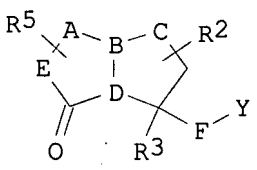
ES 2262184	T3	20061116	ES 1997-936371		19970805
US 6245764	B1	20010612	US 1998-9665		19980120 <--
US 6117896	A	20000912	US 1998-22934		19980212 <--
NO 9900522	A	19990330	NO 1999-522		19990204 <--
KR 2000029838	A	20000525	KR 1999-700994		19990205 <--
US 6372744	B1	20020416	US 2000-501052		20000209 <--
US 6699869	B1	20040302	US 2000-561107		20000428
US 2003027819	A1	20030206	US 2001-960864		20010921
US 2004230035	A1	20041118	US 2003-745471		20031222
US 7125872	B2	20061024			
US 2006293372	A1	20061228	US 2004-774043		20040205
US 2006276408	A1	20061207	US 2006-448412		20060607
PRIORITY APPLN. INFO.:			US 1996-692420	A	19960805
			US 1996-725073	A	19961002
			US 1997-797915	A	19970210
			US 1997-47067P	P	19970519
			US 1995-410518	B2	19950324
			US 1995-549006	B2	19951027
			US 1996-624690	B2	19960325
			EP 1997-936371	A3	19970805
			WO 1997-US13622	W	19970805
			US 1998-9665	A3	19980120
			US 1998-22934	A3	19980212
			US 2000-501052	A1	20000209
			US 2000-561107	A1	20000428
			US 2001-960864	B1	20010921
			US 2003-745471	A1	20031222

OTHER SOURCE(S): MARPAT 128:192934

GI



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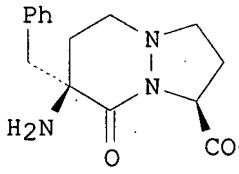


CO-L-Arg-CH_2Cl II

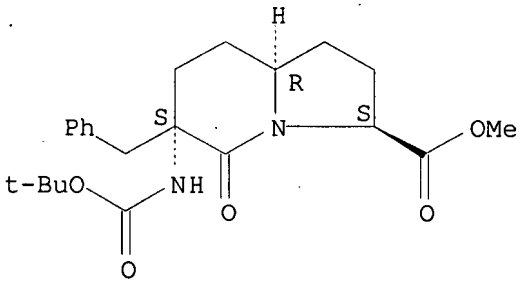
AB β-Sheet mimetics I [A = CO, (CH2)0-4, CO(CH2)1-3, (CH2)1-2CO,(CH2)1-2S; B = N, CH; C = CO, CO(CH2)1-3, (CH2)0-3, O, S, O(CH2)1-2, S(CH2)1-2; D = N, CR4; E = CR1NHZ, NZ, CR1Z; F = bond, CO; R1, R2, R4, R5 = independently amino acid side chain or derivative thereof; R2 = amino acid side chain or derivative thereof, or taken with C forms a fused substituted or unsubstituted homocyclic or heterocyclic ring; R3 = amino acid side chain or derivative thereof, or taken with C forms a bridging moiety

(CH2)1-2, O, S; Y, Z represent the remainder of the mol., with the proviso that any two adjacent CH groups of the bicyclic ring may form a double bond] and methods relating to the same are disclosed. The β-sheet mimetics have utility as protease and kinase inhibitors, as well as inhibitors of transcription factors. Methods of the invention include administration of a β-sheet mimetic, or use of the same for the manufacture of a medicament for treatment of a variety of conditions associated with the targeted protease, kinase and/or transcription factor. Thus, bicyclic peptide mimic II was prepared in several steps from phenylalanine Me ester, Et acrylate, and a protected arginine chloromethyl ketone derivative II was tested for inhibitory activity against a variety of serine proteases, and showed IC50 = 1.2 nM against thrombin in an in vitro assay.

IT 203453-43-4P 203453-44-5P 203455-59-8P
203455-60-1P
RL: RCT (Reactant); SPN (Synthetic preparation); PREP (Preparation); RACT (Reactant or reagent)
(preparation of peptide β-sheet mimetics as protease and kinase inhibitors and as inhibitors of transcription factors)

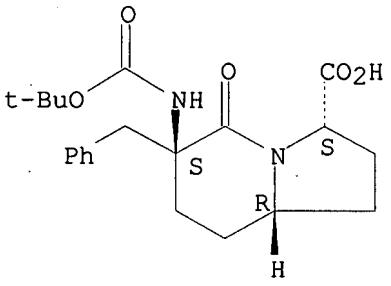
RN 203453-43-4 CAPLUS
CN 3-Indolizinecarboxylic acid, 6-[[(1,1-dimethylethoxy)carbonyl]amino]octahydro-5-oxo-6-(phenylmethyl)-, methyl ester, [3S-(3α,6β,8aβ)]- (9CI) (CA INDEX NAME)

Absolute stereochemistry.



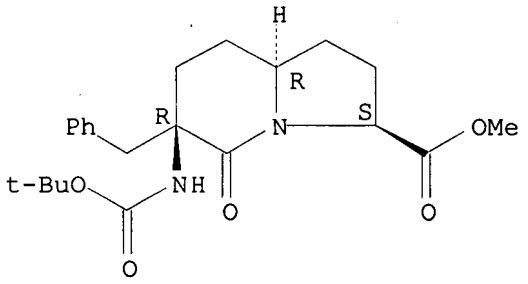
RN 203453-44-5 CAPLUS
CN 3-Indolizinecarboxylic acid, 6-[[(1,1-dimethylethoxy)carbonyl]amino]octahydro-5-oxo-6-(phenylmethyl)-, (3S,6S,8aR)- (9CI) (CA INDEX NAME)

Absolute stereochemistry.



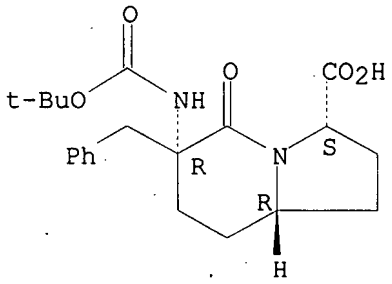
RN 203455-59-8 CAPLUS
CN 3-Indolizinecarboxylic acid, 6-[[(1,1-dimethylethoxy)carbonyl]amino]octahydro-5-oxo-6-(phenylmethyl)-, methyl ester, [3S-(3α,6α,8aβ)]- (9CI) (CA INDEX NAME)

Absolute stereochemistry.



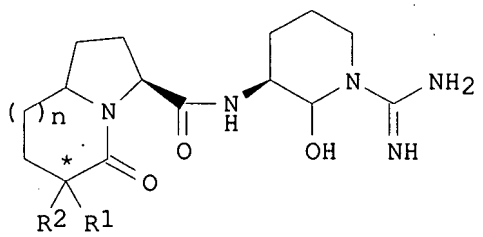
RN 203455-60-1 CAPLUS
CN 3-Indolizinecarboxylic acid, 6-[[(1,1-dimethylethoxy)carbonyl]amino]octahydro-5-oxo-6-(phenylmethyl)-, (3S,6R,8aR)- (9CI) (CA INDEX NAME)

Absolute stereochemistry.



REFERENCE COUNT: 4 THERE ARE 4 CITED REFERENCES AVAILABLE FOR THIS RECORD. ALL CITATIONS AVAILABLE IN THE RE FORMAT

L4 ANSWER 8 OF 13 CAPLUS COPYRIGHT 2007 ACS on STN
ACCESSION NUMBER: 1997:633831 CAPLUS
DOCUMENT NUMBER: 127:293616
TITLE: Design and synthesis of conformationally constrained arginal thrombin inhibitors
AUTHOR(S): Salimbeni, Aldo; Paleari, Fabio; Canevotti, Renato; Crisculoi, Marco; Lippi, Annalisa; Angiolini, Mauro; Belvisi, Laura; Scolastico, Carlo; Colombo, Lino
CORPORATE SOURCE: Lusofarmaco, Medicinal Chemistry Dep., Univ. Milano, Milan, 20132, Italy
SOURCE: Bioorganic & Medicinal Chemistry Letters (1997), 7(17), 2205-2210
CODEN: BMCLE8; ISSN: 0960-894X
PUBLISHER: Elsevier
DOCUMENT TYPE: Journal
LANGUAGE: English
GI



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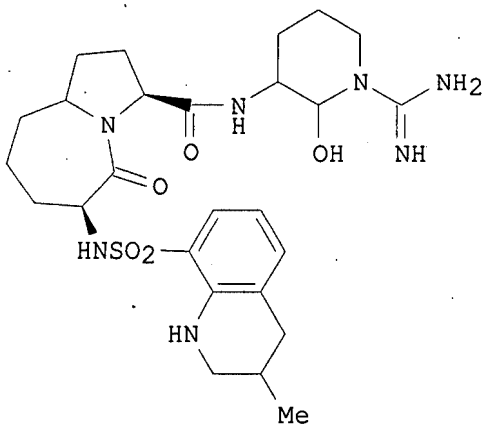


II

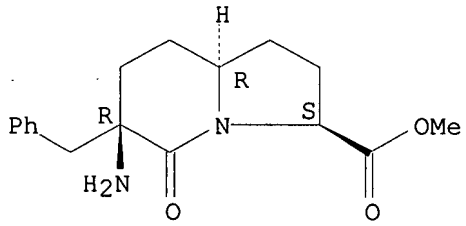
AB A series of conformationally constrained arginal thrombin inhibitors, e.g. I (R1 = PhCH2, NHAc, NHSO2CH2Ph, 1-naphthylsulfonylamino; R2 = H, CH2Ph; n = 1, 2; stereo at * center is RS, S, or R) was prepared starting from 5,6 or 5,7 bicyclic lactam structures, that an indirect approach of x-ray structure-based design indicated as D-Phe-Pro dipeptide mimetics. The tetrahydroquinolyl sulfonamido derivs. II (LR-D/009) displayed the best inhibitory potency (IC50 = 0.018 μm), with good selectivity over plasmin and trypsin.

IT 196937-03-8 196937-04-9 196937-05-0
RL: PRP (Properties)
(design and synthesis of conformationally constrained arginal thrombin inhibitors)

RN 196937-03-8 CAPLUS

CN 3-Indolizinecarboxylic acid, 6-aminooctahydro-5-oxo-6-(phenylmethyl)-, methyl ester, [3S-(3α,6α,8aβ)]- (9CI) (CA INDEX NAME)

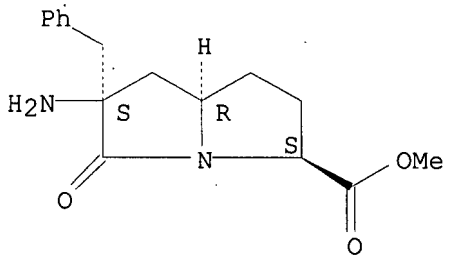
Absolute stereochemistry.



RN 196937-04-9 CAPLUS

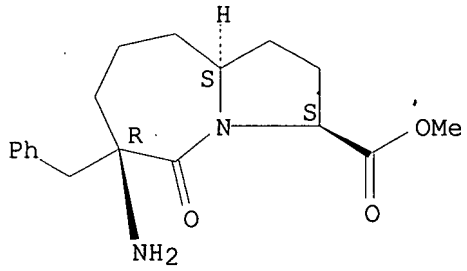
CN 1H-Pyrrolizine-3-carboxylic acid, 6-aminohexahydro-5-oxo-6-(phenylmethyl)-, methyl ester, [3S-(3α,6α,7aβ)]- (9CI) (CA INDEX NAME)

Absolute stereochemistry.



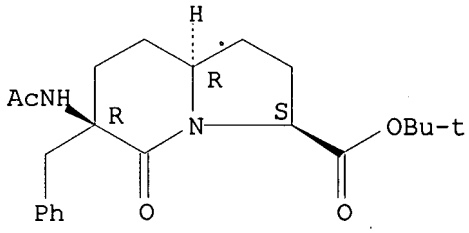
RN 196937-05-0 CAPLUS
CN 1H-Pyrrolo[1,2-a]azepine-3-carboxylic acid, 6-aminooctahydro-5-oxo-6-(phenylmethyl)-, methyl ester, (3S,6R,9aS)- (9CI) (CA INDEX NAME)

Absolute stereochemistry. Rotation (-).



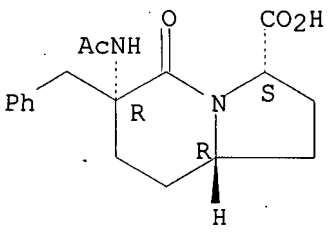
IT 162284-68-6P 188126-79-6P
RL: RCT (Reactant); SPN (Synthetic preparation); PREP (Preparation); RACT (Reactant or reagent)
(design and synthesis of conformationally constrained arginal thrombin inhibitors)
RN 162284-68-6 CAPLUS
CN 3-Indolizinecarboxylic acid, 6-(acetylamino)octahydro-5-oxo-6-(phenylmethyl)-, 1,1-dimethylethyl ester, [3S-(3α,6α,8aβ)]- (9CI) (CA INDEX NAME)

Absolute stereochemistry.



RN 188126-79-6 CAPLUS
CN 3-Indolizinecarboxylic acid, 6-(acetylamino)octahydro-5-oxo-6-(phenylmethyl)-, [3S-(3α,6α,8aβ)]- (9CI) (CA INDEX NAME)

Absolute stereochemistry.



REFERENCE COUNT: 18 THERE ARE 18 CITED REFERENCES AVAILABLE FOR THIS RECORD. ALL CITATIONS AVAILABLE IN THE RE FORMAT

L4 ANSWER 9 OF 13 CAPLUS COPYRIGHT 2007 ACS on STN
ACCESSION NUMBER: 1997:231088 CAPLUS
DOCUMENT NUMBER: 126:212450
TITLE: Preparation of arginine-containing bicyclic lactam derivatives as thrombin inhibitors
INVENTOR(S): Salimbeni, Aldo; Paleari, Fabio; Scolastico, Carlo; Criscuoli, Marco
PATENT ASSIGNEE(S): A. Menarini Industrie Farmaceutiche Riunite S.R.L., Italy; Salimbeni, Aldo; Paleari, Fabio; Scolastico, Carlo; Criscuoli, Marco
SOURCE: PCT Int. Appl., 41 pp.
CODEN: PIXXD2
DOCUMENT TYPE: Patent
LANGUAGE: English
FAMILY ACC. NUM. COUNT: 1
PATENT INFORMATION:

PATENT NO.	KIND	DATE	APPLICATION NO.	DATE
WO 9705160	A1	19970213	WO 1996-EP3167	19960718 <--
W: AL, AM, AT, AU, AZ, BB, BG, BR, BY, CA, CH, CN, CU, CZ, DE, DK, EE, ES, FI, GB, GE, HU, IL, IS, JP, KE, KG, KP, KR, KZ, LK, LR, LS, LT, LU, LV, MD, MG, MK, MN, MW, MX, NO, NZ, PL, PT, RO, RU, SD, SE				
RW: KE, LS, MW, SD, SZ, UG, AT, BE, CH, DE, DK, ES, FI, FR, GB, GR, IE, IT, LU, MC, NL, PT, SE, BF, BJ, CF, CG, CI, CM				
AU 9667342	A	19970226	AU 1996-67342	19960718 <--

PRIORITY APPLN. INFO.: IT 1995-MI1688 A 19950801
WO 1996-EP3167 W 19960718

OTHER SOURCE(S): MARPAT 126:212450
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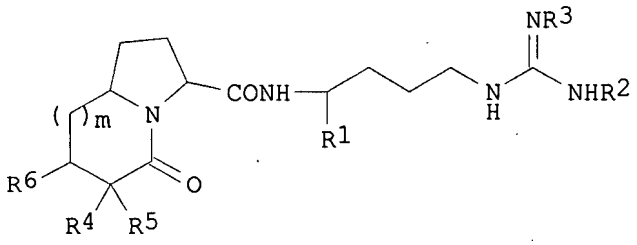

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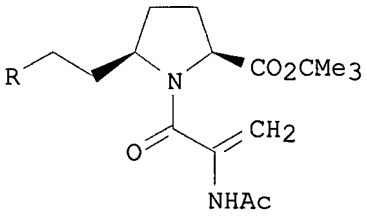
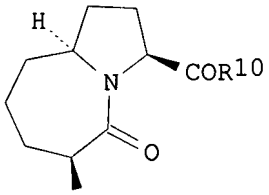


II



III

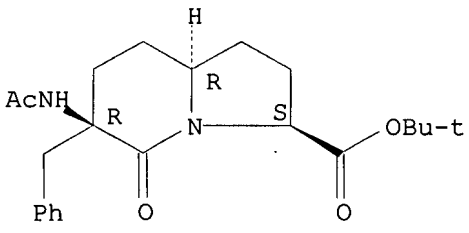
AB Bicyclic lactams containing an arginine residue, i.e. I [m = 0-3; R1 = CHO, CH2OH, CO2H, B(OH)2; R2, R3 = independently H, CO2R7, C1-4 alkyl, CH2Ph, NO2; R4, R5 = independently H, NR8R9, straight or branched C1-7 alkyl, C3-7 cycloalkyl, or an arylalkyl or heteroarylalkyl group optionally substituted by one or more groups such as halo, OMe, CF3, straight or branched C1-7 alkyl; R6 = H, straight or branched C1-7 alkyl, C3-7 cycloalkyl, or an aryl, heteroaryl, arylalkyl or heteroarylalkyl group optionally substituted by one or more groups such as halo, OMe, CF3, straight or branched C1-7 alkyl; R7 = C1-4 alkyl, CH2Ph; R8, R9 = independently H, straight or branched C1-7 alkyl, W-Q; W = CO, SO2; Q = Ph, CH2Ph, quinolyl, naphththylmethyl, tetrahydroquinolyl, optionally substituted by one or more groups such as halo, straight or branched C1-7 alkyl, OMe, CF3], which can be of use in therapy as thrombin inhibitors, are disclosed. Thus, amidation of (2S,5R)-2-tert-butoxycarbonyl-5-(2-hydroxyethyl)pyrrolidine with 2-acetylaminoacrylic acid gave 80% amide II (R = OH). Iodination of alc. II (R = OH) via its mesylate, followed by reductive radical cyclization in the presence of Bu3SnH gave octahydropyrrolo[1,2-a]azepin-5-one III (R10 = OCMe3). Deesterification of III (R10 = OCMe3) with CF3CO2H, followed by coupling with Nω-benzyloxycarbonyl-L-arginine lactam, hydride reduction, and catalytic deprotection gave arginine aldehyde derivative III (R10 = L-Arg-H).

IT 162284-68-6P 188126-64-9P 188126-66-1P
188126-68-3P 188126-74-1P 188126-79-6P
RL: RCT (Reactant); SPN (Synthetic preparation); PREP (Preparation); RACT (Reactant or reagent)
(preparation of arginine-containing bicyclic lactam derivs. as thrombin inhibitors)

RN 162284-68-6 CAPLUS

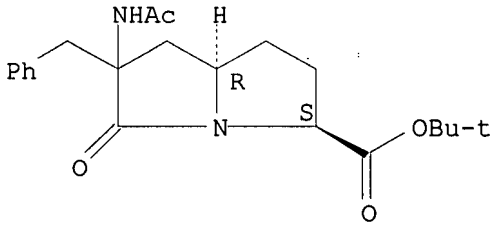
CN 3-Indolizinecarboxylic acid, 6-(acetylamino)octahydro-5-oxo-6-(phenylmethyl)-, 1,1-dimethylethyl ester, [3S-(3α,6α,8aβ)]- (9CI) (CA INDEX NAME)

Absolute stereochemistry.



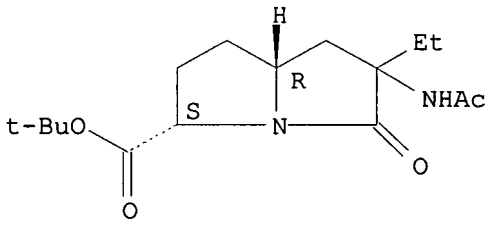
RN 188126-64-9 CAPLUS
CN 1H-Pyrrolizine-3-carboxylic acid, 6-(acetylamino)hexahydro-5-oxo-6-(phenylmethyl)-, 1,1-dimethylethyl ester, (3S,7aR)- (9CI) (CA INDEX NAME)

Absolute stereochemistry.



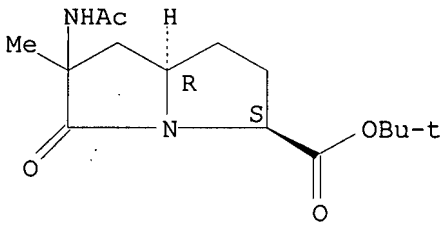
RN 188126-66-1 CAPLUS
CN 1H-Pyrrolizine-3-carboxylic acid, 6-(acetylamino)-6-ethylhexahydro-5-oxo-, 1,1-dimethylethyl ester, (3S,7aR)- (9CI) (CA INDEX NAME)

Absolute stereochemistry.



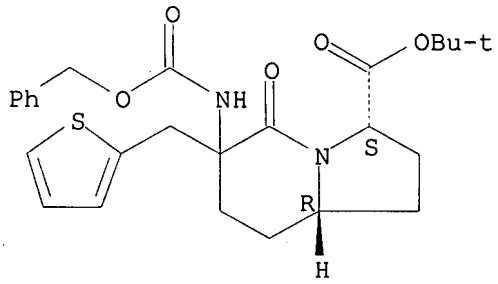
RN 188126-68-3 CAPLUS
CN 1H-Pyrrolizine-3-carboxylic acid, 6-(acetylamino)hexahydro-6-methyl-5-oxo-, 1,1-dimethylethyl ester, (3S,7aR)- (9CI) (CA INDEX NAME)

Absolute stereochemistry.



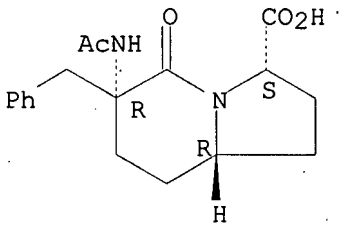
RN 188126-74-1 CAPLUS
CN 3-Indolizinecarboxylic acid, octahydro-5-oxo-6-[[(phenylmethoxy)carbonyl]amino]-6-(2-thienylmethyl)-, 1,1-dimethylethyl ester, (3S,8aR)-[partial]- (9CI) (CA INDEX NAME)

Absolute stereochemistry.



RN 188126-79-6 CAPLUS
CN 3-Indolizinecarboxylic acid, 6-(acetylamino)octahydro-5-oxo-6-(phenylmethyl)-, [3S-(3α,6α,8aβ)]- (9CI) (CA INDEX NAME)

Absolute stereochemistry.



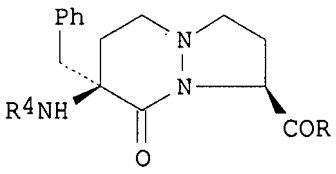
L4 ANSWER 10 OF 13 CAPLUS COPYRIGHT 2007 ACS on STN
ACCESSION NUMBER: 1996:731812 CAPLUS
DOCUMENT NUMBER: 126:8708
TITLE: Preparation of beta-sheet mimetics of peptides or proteins as protease inhibitors
INVENTOR(S): Kahn, Michael
PATENT ASSIGNEE(S): Molecumetics Ltd., USA
SOURCE: PCT Int. Appl., 141 pp.
CODEN: PIXXD2
DOCUMENT TYPE: Patent
LANGUAGE: English
FAMILY ACC. NUM. COUNT: 3
PATENT INFORMATION:

PATENT NO.	KIND	DATE	APPLICATION NO.	DATE
WO 9630396	A1	19961003	WO 1996-US4115	19960325 <--
W: AL, AM, AT, AU, AZ, BB, BG, BR, BY, CA, CH, CN, CZ, DE, DK, EE, ES, FI, GB, GE, HU, IS, JP, KE, KG, KP, KR, KZ, LK, LR, LS, LT, LU, LV, MD, MG, MK, MN, MW, MX, NO, NZ, PL, PT, RO, RU, SD, SE, SG, SI				
RW: KE, LS, MW, SD, SZ, UG, AT, BE, CH, DE, DK, ES, FI, FR, GB, GR, IE, IT, LU, MC, NL, PT, SE, BF, BJ, CF, CG, CI, CM, GA, GN				
AU 9653729	A	19961016	AU 1996-53729	19960325 <--
AU 713530	B2	19991202		
EP 815123	A1	19980107	EP 1996-910566	19960325 <--
EP 815123	B1	20011004		
R: AT, BE, CH, DE, DK, ES, FR, GB, GR, IT, LI, LU, NL, SE, MC, PT, IE, FI				
JP 10508035	T	19980804	JP 1996-529594	19960325 <--
JP 2000319295	A	20001121	JP 2000-79170	19960325 <--
AT 206433	T	20011015	AT 1996-910566	19960325 <--
US 6020331	A	20000201	US 1998-9386	19980120 <--
US 6245764	B1	20010612	US 1998-9665	19980120 <--
US 6586426	B1	20030701	US 1999-443055	19991118

US 6699869	B1	20040302	US 2000-561107		20000428
US 2003191109	A1	20031009	US 2001-8770		20011025
US 2004230035	A1	20041118	US 2003-745471		20031222
US 7125872	B2	20061024			
JP 2004131511	A	20040430	JP 2004-17703		20040126
US 2006276408	A1	20061207	US 2006-448412		20060607
PRIORITY APPLN. INFO.:			US 1995-410518	A	19950324
			US 1995-549006	A	19951027
			JP 1996-529594	A3	19960325
			JP 2000-79170	A3	19960325
			US 1996-624690	B2	19960325
			US 1996-624695	B1	19960325
			WO 1996-US4115	W	19960325
			US 1996-725073	B1	19961002
			US 1998-4968	B1	19980109
			US 1998-9386	A3	19980120
			US 1998-9665	A3	19980120
			US 2000-561107	A1	20000428
			US 2003-745471	A1	20031222

OTHER SOURCE(S): MARPAT 126:8708

GI



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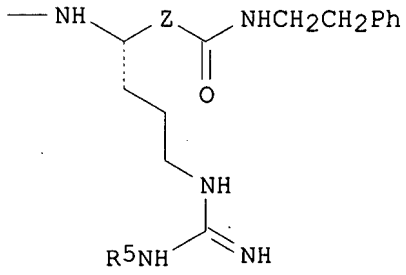
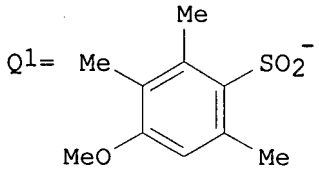
Q= 

Q1= 

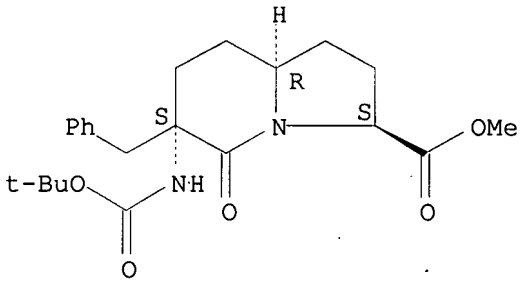
AB There are disclosed β-sheet mimetics [I; R1 - R3 = amino acid side chain moiety or its derivative; A = CO, (CH2)1-4, (CH2)1-2-O, (CH2)1-2-S; B = N, CH; C = CO, (CH2)1-3, O, S, O(CH2)1-2, S(CH2)1-2; Y, Z = the remainder of the mol.; or any 2 adjacent CH groups of the bicyclic ring may form a double bond; with the provisos that (1) R1 = an amino acid side chain moiety or derivative thereof other than H, (2) when R1 = CH2Ph, R2 = R3 = H, A = CH2CH2, and B = CH, and then C ≠ CH2, (3) when R1 = me, R2 and R3 = H, A = CH2O, B = CH, and then C ≠ CH2, and (4) when R1 = CH2Ph, R2 = R3 = H, A = CH2, B = CH, and then C ≠ S] and methods relating to the same for imparting or stabilizing the β-sheet structure of a peptide, protein or mol. In one aspect, the β-sheet mimetics are covalently attached at the end or within the length of the peptide or protein. The β-sheet mimetics have utility as protease inhibitors generally, including activity as serine protease inhibitors such as thrombin, elastase, and Factor X. Thus, diazabicyclo[4.3.0]nonane derivative (II; R = OH, R4 = Boc) (preparation given) was condensed with amino alc. (H-Q; R5 = Q1, Z = CHOH) using 1-ethyl-3-(3-dimethylaminopropyl)carbodiimide hydrochloride, HOBt hydrate, and (Me2CH)2NEt in THF to give amide alc. II (R = Q, R5 = Q1, Z = CHOH, R4 = Boc), which was oxidized by Dess-Martin periodinane in CH2Cl2 and deprotected with 95% aqueous CF3CO2H and thioanisole to give the β-sheet mimetic II (R = Q, R5 = H, Z = CO, R4 = H). The latter compound in vitro inhibited various serine proteases such as

thrombin, factor VII, factor X, and trypsin, e.g. with Ki of 7.10 + 10-11 M for thrombin.

IT 183442-92-4P 183442-93-5P 183442-97-9P
183624-03-5P
RL: RCT (Reactant); SPN (Synthetic preparation); PREP (Preparation); RACT (Reactant or reagent)
(preparation of beta-sheet mimetics of peptides or proteins as protease inhibitors)

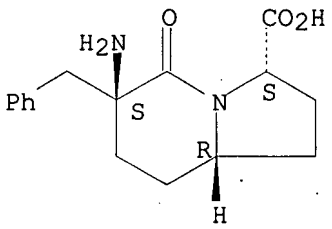
RN 183442-92-4 CAPLUS
CN 3-Indolizinecarboxylic acid, 6-[[(1,1-dimethylethoxy)carbonyl]amino]octahydro-5-oxo-6-(phenylmethyl)-, methyl ester, (3R,6R,8aS)-rel- (9CI) (CA INDEX NAME)

Relative stereochemistry.



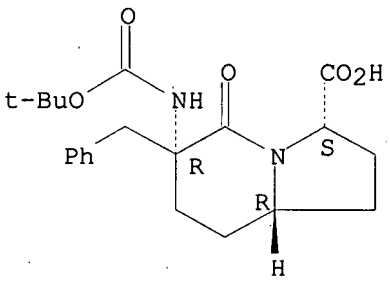
RN 183442-93-5 CAPLUS
CN 3-Indolizinecarboxylic acid, 6-aminooctahydro-5-oxo-6-(phenylmethyl)-, (3R,6R,8aS)-rel- (9CI) (CA INDEX NAME)

Relative stereochemistry.



RN 183442-97-9 CAPLUS
CN 3-Indolizinecarboxylic acid, 6-[[(1,1-dimethylethoxy)carbonyl]amino]octahydro-5-oxo-6-(phenylmethyl)-, (3α,6α,8aβ)- (9CI) (CA INDEX NAME)

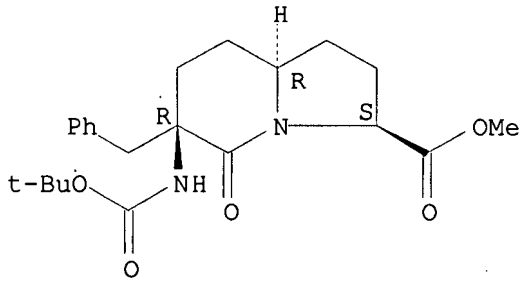
Relative stereochemistry.



RN 183624-03-5 CAPLUS
CN 3-Indolizinecarboxylic acid, 6-[[(1,1-dimethylethoxy)carbonyl]amino]octahydro-5-oxo-6-(phenylmethyl)-, methyl ester, (3R,6S,8aS)-rel- (9CI) (CA

INDEX NAME)

Relative stereochemistry.



L4 ANSWER 11 OF 13 CAPLUS COPYRIGHT 2007 ACS on STN
ACCESSION NUMBER: 1996:731810 CAPLUS
DOCUMENT NUMBER: 126:8707
TITLE: Preparation of beta-sheet mimetics of peptides or proteins as inhibitors of biologically active peptides or proteins
INVENTOR(S): Kahn, Michael
PATENT ASSIGNEE(S): Molecumetics Ltd., USA
SOURCE: PCT Int. Appl., 158 pp.
CODEN: PIXXD2
DOCUMENT TYPE: Patent
LANGUAGE: English
FAMILY ACC. NUM. COUNT: 3
PATENT INFORMATION:

PATENT NO.	KIND	DATE	APPLICATION NO.	DATE
WO 9630035	A1	19961003	WO 1996-US4044	19960325 <--
W: AL, AM, AT, AU, AZ, BB, BG, BR, BY, CA, CH, CN, CZ, DE, DK, EE, ES, FI, GB, GE, HU, IS, JP, KE, KG, KP, KR, KZ, LK, LR, LS, LT, LU, LV, MD, MG, MK, MN, MW, MX, NO, NZ, PL, PT, RO, RU, SD, SE, SG, SI				
RW: KE, LS, MW, SD, SZ, UG, AT, BE, CH, DE, DK, ES, FI, FR, GB, GR, IE, IT, LU, MC, NL, PT, SE, BF, BJ, CF, CG, CI, CM, GA, GN				
CA 2215695	A1	19961003	CA 1996-2215695	19960325 <--
CA 2215695	C	20030916		
CA 2215720	A1	19961003	CA 1996-2215720	19960325 <--
AU 9653714	A	19961016	AU 1996-53714	19960325 <--
AU 712581	B2	19991111		
EP 817642	A1	19980114	EP 1996-910547	19960325 <--
R: AT, BE, CH, DE, DK, ES, FR, GB, GR, IT, LI, LU, NL, SE, MC, PT, IE, FI				
JP 10508034	T	19980804	JP 1996-529567	19960325 <--
JP 2000319295	A	20001121	JP 2000-79170	19960325 <--
ES 2161354	T3	20011201	ES 1996-910566	19960325 <--
US 6020331	A	20000201	US 1998-9386	19980120 <--
US 6245764	B1	20010612	US 1998-9665	19980120 <--
US 6586426	B1	20030701	US 1999-443055	19991118
US 6699869	B1	20040302	US 2000-561107	20000428
US 2003191109	A1	20031009	US 2001-8770	20011025
US 2004230035	A1	20041118	US 2003-745471	20031222
US 7125872	B2	20061024		
JP 2004131511	A	20040430	JP 2004-17703	20040126
US 2006276408	A1	20061207	US 2006-448412	20060607

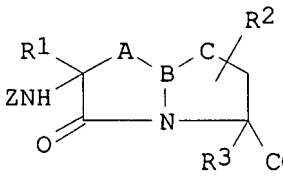
PRIORITY APPLN. INFO.:

US 1995-410518	A	19950324
US 1995-549006	A	19951027
JP 1996-529594	A3	19960325
JP 2000-79170	A3	19960325

US 1996-624690	B2	19960325
US 1996-624695	B1	19960325
WO 1996-US4044	W	19960325
US 1996-725073	B1	19961002
US 1998-4968	B1	19980109
US 1998-9386	A3	19980120
US 1998-9665	A3	19980120
US 2000-561107	A1	20000428
US 2003-745471	A1	20031222

OTHER SOURCE(S): MARPAT 126:8707

GI



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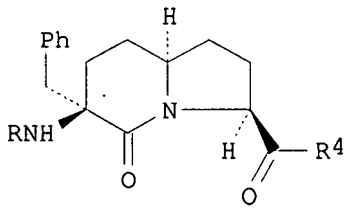

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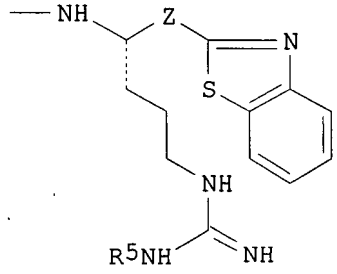
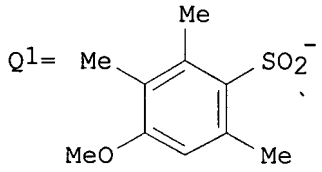


Q1=



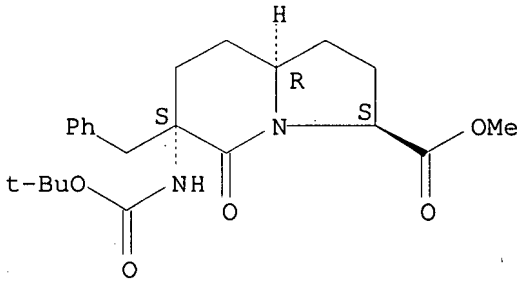
AB There are disclosed β-sheet mimetics [I; R1 - R3 = amino acid side chain moiety or its derivative; A = CO, (CH2)1-4, (CH2)1-2-O, (CH2)1-2-S; B = N, CH; C = CO, (CH2)1-3, O, S, O(CH2)1-2, S(CH2)1-2; Y, Z = the remainder of the mol.; or any 2 adjacent CH groups of the bicyclic ring may form a double bond] and methods relating to the same for imparting or stabilizing the β-sheet structure of a peptide, protein or mol. In one aspect, the β-sheet mimetics are covalently attached at the end or within the length of the peptide or protein. The β-sheet mimetics have utility as inhibitors of one or more of proteases, kinases, CAAX motif (Ras prenylation of the Cys within its C-terminal CAAX sequence by farnesyl transferase, wherein "A" is defined as an amino acid with a hydrophobic side chain and "X" is another amino acid), peptides binding to SH2 domains, and MHC-I and/or MHC-II (major histocompatibility complex class I and class II) presentation of peptides to T cell receptors in warm-blooded animals. Thus, azabicyclo[4.3.0]nonane derivative (II; R = Boc, R4 = OH) (preparation given) was condensed with benzothiazolylarginol derivative (H-Q.CF3CO2H; R5 = Q1, Z = CHOH) using 1-ethyl-3-(3-dimethylaminopropyl)carbodiimide hydrochloride, HOBt, and (Me2CH)2NEt in THF to give arginol derivative II (R = Boc, R4 = Q, R5 = Q1 Z = CHOH), which was oxidized by Dess-Martin periodinane in CH2Cl2 to arginine derivative II (R = Boc, R4 = Q, R5 = Q1 Z = CO) and deprotected 95% aqueous CF3CO2H and thioanisole at room temperature for 20 h to give, after HPLC purification, the β-sheet mimetic II (R = H, R4 = Q, R5 = H, Z = CO). The latter compound in vitro inhibited various serine proteases such as thrombin, factor VII, factor X, factor XI, urokinase, thrombin-thrombomodulin complex, activated protein C, plasmin, tissue plasminogen activator, trypsin, and tryptase, e.g. with Ki of 8.50 + 10-11 M for thrombin.

IT 183442-92-4P 183442-93-5P 183442-97-9P
183624-03-5P

RL: RCT (Reactant); SPN (Synthetic preparation); PREP (Preparation); RACT (Reactant or reagent)
(preparation of beta-sheet mimetics of peptides or proteins as inhibitors of biol. active peptides or proteins)

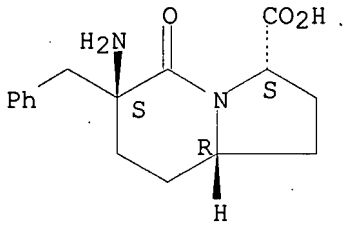
RN 183442-92-4 CAPLUS
CN 3-Indolizinecarboxylic acid, 6-[[(1,1-dimethylethoxy)carbonyl]amino]octahydro-5-oxo-6-(phenylmethyl)-, methyl ester, (3R,6R,8aS)-rel- (9CI) (CA INDEX NAME)

Relative stereochemistry.



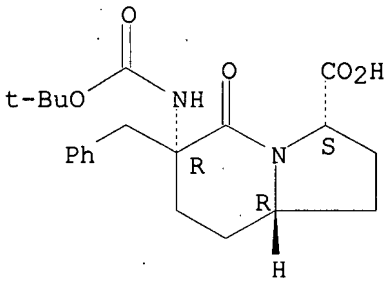
RN 183442-93-5 CAPLUS
CN 3-Indolizinecarboxylic acid, 6-aminooctahydro-5-oxo-6-(phenylmethyl)-, (3R,6R,8aS)-rel- (9CI) (CA INDEX NAME)

Relative stereochemistry.



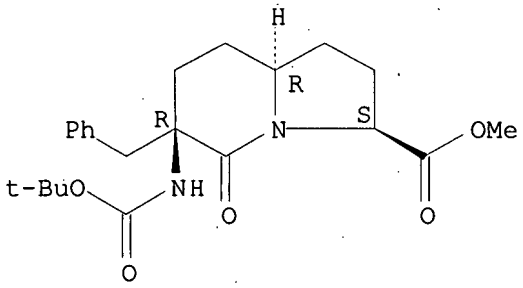
RN 183442-97-9 CAPLUS
CN 3-Indolizinecarboxylic acid, 6-[[(1,1-dimethylethoxy)carbonyl]amino]octahydro-5-oxo-6-(phenylmethyl)-, (3α,6α,8aβ)- (9CI) (CA INDEX NAME)

Relative stereochemistry.

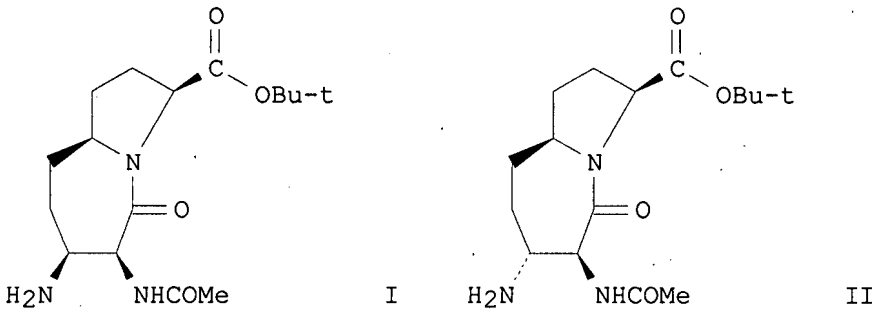


RN 183624-03-5 CAPLUS
CN 3-Indolizinecarboxylic acid, 6-[[(1,1-dimethylethoxy)carbonyl]amino]octahydro-5-oxo-6-(phenylmethyl)-, methyl ester, (3R,6S,8aS)-rel- (9CI) (CA INDEX NAME)

Relative stereochemistry.



L4 ANSWER 12 OF 13 CAPLUS COPYRIGHT 2007 ACS on STN
ACCESSION NUMBER: 1996:662548 CAPLUS
DOCUMENT NUMBER: 126:19211
TITLE: Conformationally constrained dipeptides: synthesis of bicyclic lactams by stereoselective radical cyclizations
AUTHOR(S): Colombo, Lino; Di Giacomo, Marcello; Belvisi, Laura; Manzoni, Leonardo; Scolastico, Carlo; Salimbeni, Aldo
CORPORATE SOURCE: Dip. Chim. Farmaceutica, Univ. Pavia, Pavia, I-27100, Italy
SOURCE: Gazzetta Chimica Italiana (1996), 126(8), 543-554
CODEN: GCITA9; ISSN: 0016-5603
PUBLISHER: Societa Chimica Italiana
DOCUMENT TYPE: Journal
LANGUAGE: English
OTHER SOURCE(S): CASREACT 126:19211
GI



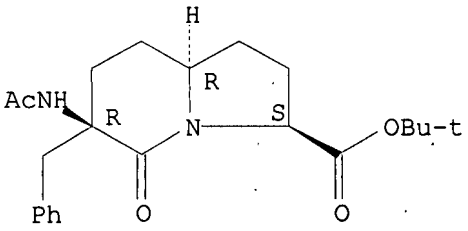
AB Regioselective and stereoselective radical cyclization of β-substituted α-N-acetyl acrylamides was performed. This method led to the formation of 6,5- and 7,5-fused bicyclic lactams, which can be viewed as conformationally restricted dipeptide mimics. The peptide mimics I and II were prepared

IT 162284-68-6P
RL: SPN (Synthetic preparation); PREP (Preparation)
(preparation of conformationally constrained dipeptide mimics by radical cyclization of β-substituted α-N-acetyl acrylamides)

RN 162284-68-6 CAPLUS

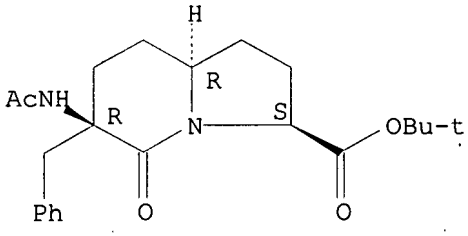
CN 3-Indolizinecarboxylic acid, 6-(acetylamino)octahydro-5-oxo-6-(phenylmethyl)-, 1,1-dimethylethyl ester, [3S-(3α,6α,8aβ)]- (9CI) (CA INDEX NAME)

Absolute stereochemistry.



L4 ANSWER 13 OF 13 CAPLUS COPYRIGHT 2007 ACS on STN
ACCESSION NUMBER: 1995:357314 CAPLUS
DOCUMENT NUMBER: 122:240379
TITLE: Conformationally constrained dipeptides: synthesis of 7,5- and 6,5-fused bicyclic lactams by stereoselective radical cyclizations
AUTHOR(S): Colombo, Lino; Di Giacomo, Marcello; Scolastico, Carlo; Manzoni, Leonardo; Belvisi, Laura; Molteni, Valentina
CORPORATE SOURCE: Dipart. Chim. Farm., Univ. Pavia, Pavia, I-27100, Italy
SOURCE: Tetrahedron Letters (1995), 36(4), 625-8
CODEN: TELEAY; ISSN: 0040-4039
PUBLISHER: Elsevier
DOCUMENT TYPE: Journal
LANGUAGE: English
OTHER SOURCE(S): CASREACT 122:240379
AB A study of radical cyclizations of β-substituted α-N-acetyl acrylamide have been performed: high level of regio- and stereoselectivity was obtained.
IT 162284-68-6P
RL: SPN (Synthetic preparation); PREP (Preparation)
(conformationally constrained dipeptides and synthesis of fused bicyclic lactams by stereoselective radical cyclizations)
RN 162284-68-6 CAPLUS
CN 3-Indolizinecarboxylic acid, 6-(acetylamino)octahydro-5-oxo-6-(phenylmethyl)-, 1,1-dimethylethyl ester, [3S-(3α,6α,8aβ)]- (9CI) (CA INDEX NAME)

Absolute stereochemistry.



=> FIL STNGUIDE

COST IN U.S. DOLLARS	SINCE FILE ENTRY	TOTAL SESSION
FULL ESTIMATED COST	71.46	243.77
DISCOUNT AMOUNTS (FOR QUALIFYING ACCOUNTS)	SINCE FILE ENTRY	TOTAL SESSION
CA SUBSCRIBER PRICE	-10.14	-10.14

FILE 'STNGUIDE' ENTERED AT 11:17:53 ON 02 JUL 2007

FILE CONTAINS CURRENT INFORMATION.
LAST RELOADED: Jun 29, 2007 (20070629/UP).

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(FILE 'HOME' ENTERED AT 11:16:18 ON 02 JUL 2007)

FILE 'REGISTRY' ENTERED AT 11:16:27 ON 02 JUL 2007
L1 STRUCTURE UPLOADED
L2 43 S L1 FULL

FILE 'CAPLUS' ENTERED AT 11:16:54 ON 02 JUL 2007
L3 18 S L2 FULL
L4 13 S L3 AND PY<2003

FILE 'STNGUIDE' ENTERED AT 11:17:53 ON 02 JUL 2007

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COST IN U.S. DOLLARS	SINCE FILE ENTRY	TOTAL SESSION
FULL ESTIMATED COST	0.24	244.01

DISCOUNT AMOUNTS (FOR QUALIFYING ACCOUNTS)	SINCE FILE ENTRY	TOTAL SESSION
CA SUBSCRIBER PRICE	0.00	-10.14

STN INTERNATIONAL LOGOFF AT 11:20:34 ON 02 JUL 2007